WHAT IS CLAIMED:

1. A method of culturing peripheral lymphoid organ cells comprising:

culturing peripheral lymphoid organ cells on a three-dimensional scaffolding which is covered or surrounded with culture medium under conditions effective to generate and maintain mature and functional peripheral lymphoid organ cells, wherein said three-dimensional scaffolding allows cells in the culture medium to have cell to cell contact in three dimensions.

2. The method according to claim 1, wherein the scaffolding is selected from the group consisting of tangled fibers, porous particles, sponge, sponge-like material, and combinations thereof.

3. The method according to claim 1, wherein the scaffolding is formed from a material selected from the group consisting of metal, glass, ceramic, plastic, hydroxyapatite, treated or untreated bone, a synthetic polymer, a natural substance, a semisynthetic material, and combinations thereof.

4. The method according to claim 3, wherein the material is degradable.

5. The method according to claim 3, wherein the material is non-degradable.

6. The method according to claim 1, wherein the culture medium contains exogenous growth factors, cytokines, lymphokines, hormones, chemokines, interleukins, mitogens, antigens or antigenic fragments thereof, or combination thereof.

7. The method according to claim 6, wherein the culture medium contains cytokines which are selected from the group consisting of interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-7, interleukin-12, flt-3 Ligand,

stem cell factor, thrombopoietin, CD40 ligand, BAC-1, L-BCGF, soluble interleukin 6R, and combinations thereof.

8. The method according to claim 6, wherein the culture medium contains an antigen which is selected from the group consisting of a peptide, protein, carbohydrate, glycoprotein, proteoglycan, lipopolysaccharide, nucleic acid, virus, cells, cell fragment, tissue, and combination thereof.

9. The method according to claim 8, wherein the antigen is a tumor antigen.

10. The method according to claim 6, wherein the culture medium contains antigens and antigenic fragments that are presented by antigen presenting cells.

11. The method according to claim 10, wherein the antigen presenting cells are dendritic cells.

12. The method according to claim 6, wherein the culture medium contains antigens or antigenic fragments that are present as a conjugate.

13. The method according to claim 1, wherein the peripheral lymphoid organ cells are B-cells, T-cells, or combination thereof.

14. The method according to claim 13, wherein the peripheral lymphoid organ cells are T-cells which are selected from the group consisting of cytotoxic T-cells, helper T-cells, and combination thereof.

15. The method according to the claim 13, wherein the peripheral lymphoid organ cells are B-cells which are selected from the group consisting of immature B cells, naïve B cells, memory B-cells, B1 cells, B2 cells, plasma cells, and combination thereof.

16. The method according to claim 1, wherein the peripheral lymphoid organ cells are selected from the group consisting of natural killer (NK) cells, dendritic and follicular dendritic cells, granulocytes, macrophages, and stromal cell subsets.

17. The method according to claim 1, wherein the cultured peripheral lymphoid organ cells are selected from the group consisting of spleen cells, lymph node cells, thymus cells, Peyer's patches cells, and combinations thereof.

18. The method according to claim 17, wherein the cultured peripheral lymphoid organ cells are spleen cells.

19. The method according to claim 1, wherein the cultured peripheral lymphoid organ cells express a surface marker selected from the group consisting of CD5, CD23, CD69, CD25, MHC class I or II, CD80/86, CD138, CD38, CD27, CD8, CD4, CD3, CD45-RO, CD45-RA, and combinations thereof.

20. The method according to claim 1, wherein the cultured peripheral lymphoid organ cells fail to express a surface marker selected from the group consisting of CD5, CD23, CD69, CD25, MHC class I or II, CD80/86, CD138, CD38, CD27, CD8, CD4, CD3, CD45-RO, CD45-RA, and combinations thereof.

21. The method according to claim 1, wherein said culturing is carried out without addition of external mitogens.

22. The method according to claim 1 further comprising:

seeding or reseeding the culture medium with peripheral lymphoid organ cells, peripheral lymphoid cells, primary lymphoid organ cells, stem cells, or combinations thereof.

23. The method according to claim 22, wherein the culture medium is reseeded with peripheral lymphoid organ cells selected from the group consisting of spleen cells, lymph node cells, Peyer's patches cells, and combinations thereof.

24. The method according to claim 1, wherein said culturing is carried out with an antigen or antigenic fragment thereof in the culture medium and under conditions effective to produce antigen-specific lymphocytes.

25. The method according to claim 24, wherein said culturing is carried out under conditions effective to permit clonal selection, expansion, and/or affinity maturation of lymphocytes.

26. The method according to claim 24, further comprising:
adding an adjuvant to the cell culture.

27. The method according to claim 24, wherein the antigen is selected from the group consisting of a peptide, protein, carbohydrate, glycoprotein, proteoglycan, lipopolysaccharide, nucleic acid, virus, cells, cell fragment, tissue, and combinations thereof.

28. The method according to claim 24, wherein the antigen is a tumor antigen.

29. The method according to claim 24, wherein the antigen or antigenic fragment are presented by antigen presenting cells.

30. The method according to claim 24, wherein the antigen or antigenic fragment are present as a conjugate.

31. The method according to claim 24, wherein said culturing is carried out under conditions effective to permit the antigen-specific lymphocytes to produce antibodies.

32. The method according to claim 24 further comprising:
immortalizing the antigen-specific lymphocytes.

33. The method according to claim 32, wherein the lymphocytes are B-cells, T-cells, or combinations thereof.

34. The method according to claim 32, wherein said immortalizing is induced.

35. The method according to claim 34, wherein said immortalizing comprises:

fusing the antigen-specific lymphocytes to a cell line under conditions effective to produce a hybridoma cell line.

36. The method according to claim 35 further comprising:

recovering monoclonal antibodies from the hybridoma cell line.

37. The method according to claim 32, wherein said immortalizing is spontaneous.

38. A method of screening for vaccine candidates for efficacy in eliciting an immune response comprising:

culturing peripheral lymphoid organ cells in a container on a three-dimensional scaffolding which is covered or surrounded with culture medium under conditions effective to generate and maintain mature and functional peripheral lymphoid organ cells, wherein said three-dimensional scaffolding allows the peripheral lymphoid organ cells in the culture medium to have cell to cell contact in three dimensions.

adding a vaccine candidate to the container; and

determining whether the vaccine candidate elicits an immune response in the cultured peripheral lymphoid organ cells.

39. The method according to claim 38, wherein the cells are mammalian peripheral lymphoid organ cells.

40. The method according to claim 39, wherein the mammalian peripheral lymphoid organ cells are human cells.

41. The method according to claim 38, wherein the culture medium contains exogenous growth factors, cytokines, lymphokines, hormones, chemokines, interleukins, mitogens, antigens or antigenic fragments thereof, or combinations thereof.

42. The method according to claim 41, wherein the culture medium contains cytokines which are selected from the group consisting of interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-7, interleukin-12, flt-3 Ligand, stem cell factor, thrombopoietin, CD40 ligand, BAC-1, L-BCGF, soluble interleukin 6R, and combinations thereof.

43. The method according to claim 41, wherein the culture medium contains an antigen which is selected from the group consisting of a peptide, protein, glycoprotein, proteoglycan, lipopolysaccharide, nucleic acid, virus, cells, cell fragment, tissue, and combinations thereof.

44. The method according to claim 38, wherein the peripheral lymphoid organ cells are B-cells, T-cells, or combinations thereof.

45. The method according to claim 44, wherein the peripheral lymphoid organ cells are T-cells which are selected from the group consisting of cytotoxic T-cells, helper T-cells, and combinations thereof.

46. The method according to the claim 44, wherein the peripheral lymphoid organ cells are B-cells which are selected from the group consisting of immature B cells, naïve B cells, memory B-cells, B1 cells, B2 cells, plasma cells, and combinations thereof.

47. The method according to claim 38, wherein the cultured peripheral lymphoid organ cells are selected from the group consisting of spleen cells, lymph node cells, thymus cells, Peyer's patches cells, and combinations thereof.

48. The method according to claim 47, wherein the cultured peripheral lymphoid organ cells are spleen cells.

49. The method according to claim 47, wherein the cultured peripheral lymphoid organ cells are lymph node cells.

50. The method according to claim 38, wherein the cultured peripheral lymphoid organ cells express a surface marker selected from the group consisting of CD5, CD23, CD69, CD25, MHC class I or II, CD80/86, CD138, CD38, CD27, CD8, CD4, CD3, CD45-RO, CD45-RA, and combinations thereof.

51. The method according to claim 38, wherein the cultured peripheral lymphoid organ cells fail to express a surface marker selected from the group consisting of CD5, CD23, CD69, CD25, MHC class I or II, CD80/86, CD138, CD38, CD27, CD8, CD4, CD3, CD45-RO, CD45-RA, and combinations thereof.

52. The method according to claim 38, wherein the scaffolding is selected from the group consisting of tangled fibers, porous particles, sponge, sponge-like material, and combinations thereof.

53. The method according to claim 38, wherein the scaffolding is formed from a material selected from the group consisting of a synthetic polymer, a natural substance, a semisynthetic material, and combinations thereof.

54. The method according to claim 53, wherein the material is degradable.

55. The method according to claim 53, wherein the material is non-degradable.

56. The method according to claim 38, wherein said culturing is carried out without addition of external mitogens.

57. The method according to claim 38 further comprising:

seeding or reseeding the culture medium with peripheral lymphoid organ cells, peripheral lymphoid cells, primary lymphoid organ cells, stem cells, or combinations thereof.

58. The method according to claim 57, wherein the culture medium is reseeded with peripheral lymphoid organ cells selected from the group consisting of spleen cells, lymph node cells, Peyer's patches cells, and combinations thereof.

59. A method of identifying genes or proteins which are related to peripheral lymphoid organ cell formation or function which comprises:

culturing peripheral lymphoid organ cells on a three-dimensional scaffolding which is covered or surrounded with culture medium under conditions effective to generate and maintain mature and functional peripheral lymphoid organ cells, wherein said three-dimensional scaffolding allows the cells in the culture medium to have cell to cell contact in three dimensions.

altering one or more culture conditions in a test culture;

determining peripheral lymphoid organ cell number and function in the test culture; and

screening for genes or proteins associated with a change in peripheral lymphoid organ cell number or function in the test culture.

60. The method according to claim 59, wherein cell number is determined by immunohistochemistry, cell morphology, or flow cytometry.

61. The method according to claim 59, wherein said screening for proteins or genes associated with change in peripheral lymphoid cell number or function involves at least one of differential display, RNA arbitrarily primed (RAP)-PCR, or microarray analysis.

62. The method according to claim 59, wherein the peripheral lymphoid organ cells are mammalian peripheral lymphoid organ cells.

63. The method according to claim 62, wherein the mammalian peripheral lymphoid organ cells are human cells.

64. The method according to claim 59, wherein the culture medium contains exogenous growth factors, cytokines, lymphokines, hormones, chemokines, interleukins, mitogens, antigens or antigenic fragments thereof, or combinations thereof.

65. The method according to claim 64, wherein the culture medium contains cytokines which are selected from the group consisting of interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-7, interleukin-12, flt-3 Ligand, stem cell factor, thrombopoietin, CD40 ligand, BAC-1, L-BCGF, soluble interleukin 6R, and combinations thereof.

66. The method according to claim 64, wherein the culture medium contains an antigen which is selected from the group consisting of a peptide, protein, carbohydrate, glycoprotein, proteoglycan, lipopolysaccharide, nucleic acid, virus, cells, cell fragment, tissue, and combinations thereof.

67. The method according to claim 59, wherein the peripheral lymphoid organ cells are B-cells, T-cells, or combinations thereof.

68. The method according to claim 67, wherein the peripheral lymphoid organ cells are T-cells which are selected from the group consisting of cytotoxic T-cells, helper T-cells, and combinations thereof.

69. The method according to the claim 67, wherein the peripheral lymphoid organ cells are B-cells which are selected from the group consisting of immature B cells, naïve B cells, memory B-cells, B1 cells, B2 cells, plasma cells, and combinations thereof.

70. The method according to claim 59, wherein the cultured peripheral lymphoid organ cells are selected from the group consisting of spleen cells, lymph node cells, thymus cells, Peyer's patches cells, and combinations thereof.

71. The method according to claim 70, wherein the cultured peripheral lymphoid organ cells are spleen cells.

72. The method according to claim 40, wherein the cultured peripheral lymphoid organ cells are lymph node cells.

73. The method according to claim 59, wherein the cultured peripheral lymphoid organ cells express a surface marker selected from the group consisting of CD5, CD23, CD69, CD25, MHC class I or II, CD80/86, CD138, CD38, CD27, CD8, CD4, CD3, CD45-RO, CD45-RA, and combinations thereof.

74. The method according to claim 59, wherein the cultured peripheral lymphoid organ cells fail to express a surface marker selected from the group consisting of CD5, CD23, CD69, CD25, MHC class I or II, CD80/86, CD138, CD38, CD27, CD8, CD4, CD3, CD45-RO, CD45-RA, and combinations thereof.

75. The method according to claim 59, wherein the scaffolding is selected from the group consisting of tangled fibers, porous particles, sponge, sponge-like material, and combinations thereof.

76. The method according to claim 59, wherein the scaffolding is formed from a material selected from the group consisting of a synthetic polymer, a natural substance, a semisynthetic material, and combinations thereof.

77. The method according to claim 76, wherein the material is degradable.

78. The method according to claim 76, wherein the material is non-degradable.

79. The method according to claim 59, wherein said culturing is carried out without addition of external mitogens.

80. The method according to claim 59 further comprising:

seeding or reseeding the culture medium with peripheral lymphoid organ cells, peripheral lymphoid cells, primary lymphoid organ cells, stem cells, or combinations thereof.

81. The method according to claim 80, wherein the culture medium is reseeded with peripheral lymphoid organ cells selected from the group consisting of spleen cells, lymph node cells, Peyer's patches cells, and combinations thereof.

82. A method of screening for drugs effecting peripheral lymphoid organ cell generation, maturation or function which comprises:

culturing peripheral lymphoid organ cells in a container on a three-dimensional scaffolding which is covered or surrounded with culture medium under conditions effective to generate and maintain mature and functional peripheral lymphoid organ cells, wherein said three-dimensional scaffolding allows the cells in the culture medium to have cell to cell contact in three dimensions.

adding a test compound to the container,

removing cultured cells from the container; and

determining the test compound's ability to effect lymphoid cell generation, maturation or function.

83. The method according to claim 82, wherein the ability of a test compound to effect peripheral lymphoid cell generation, maturation or function is determined by lymphoid peripheral cell count, immunohistochemistry, flow cytometry, or a combination thereof.

84. The method according to claim 82, wherein the test compound stimulates peripheral lymphoid organ cell maturation.

85. The method according to claim 82, wherein the test compound inhibits peripheral lymphoid organ cell maturation.

86. The method according to claim 82, wherein the cells are mammalian peripheral lymphoid organ cells.

87. The method according to claim 86, wherein the mammalian peripheral lymphoid organ cells are human cells.

88. The method according to claim 82, wherein the culture medium contains exogenous growth factors, cytokines, lymphokines, hormones, chemokines, interleukins, mitogens, antigens or antigenic fragments thereof, or combinations thereof.

89. The method according to claim 88, wherein the culture medium contains cytokines which are selected from the group consisting of interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-7, interleukin-12, flt-3 Ligand, stem cell factor, thrombopoietin, CD40 ligand, BAC-1, L-BCGF, soluble interleukin 6R, and combinations thereof.

90. The method according to claim 88, wherein the culture medium contains an antigen which is selected from the group consisting of a peptide, protein, carbohydrate, glycoprotein, proteoglycan, lipopolysaccharide, nucleic acid, virus, cells, cell fragment, tissue, and combinations thereof.

91. The method according to claim 82, wherein the peripheral lymphoid organ cells are B-cells, T-cells, or combinations thereof.

92. The method according to claim 91, wherein the peripheral lymphoid organ cells are T-cells which are selected from the group consisting of cytotoxic T-cells, helper T-cells, and combinations thereof.

93. The method according to the claim 91, wherein the peripheral lymphoid organ cells are B-cells which are selected from the group consisting of immature B cells, naïve B cells, memory B-cells, B1 cells, B2 cells, plasma cells, and combinations thereof.

94. The method according to claim 82, wherein the cultured peripheral lymphoid organ cells are selected from the group consisting of spleen cells, lymph node cells, thymus cells, Peyer's patches cells, and combinations thereof.

95. The method according to claim 94, wherein the cultured peripheral lymphoid organ cells are spleen cells.

96. The method according to claim 94, wherein the cultured peripheral lymphoid organ cells are lymph node cells.

97. The method according to claim 82, wherein the cultured peripheral lymphoid organ cells express a surface marker selected from the group consisting of CD5, CD23, CD69, CD25, MHC class I or II, CD80/86, CD138, CD38, CD27, CD8, CD4, CD3, CD45-RO, CD45-RA, and combinations thereof.

98. The method according to claim 82, wherein the cultured peripheral lymphoid organ cells fail to express a surface marker selected from the group consisting of CD5, CD23, CD69, CD25, MHC class I or II, CD80/86, CD138, CD38, CD27, CD8, CD4, CD3, CD45-RO, CD45-RA, and combinations thereof.

99. The method according to claim 82, wherein the scaffolding is selected from the group consisting of tangled fibers, porous particles, sponge, sponge-like material, and combinations thereof.

100. The method according to claim 82, wherein the scaffolding is formed from a material selected from the group consisting of a synthetic polymer, a natural substance, a semisynthetic material, and combinations thereof.

101. The method according to claim 100, wherein the material is degradable.

102. The method according to claim 100, wherein the material is non-degradable.

103. The method according to claim 82, wherein said culturing is carried out without addition of external mitogens.

104. The method according to claim 82 further comprising:

seeding or reseeding the culture medium with peripheral lymphoid organ cells, peripheral lymphoid cells, primary lymphoid organ cells, stem cells, or combinations thereof.

105. The method according to claim 104, wherein the culture medium is reseeded with peripheral lymphoid organ cells selected from the group consisting of spleen cells, lymph node cells, Peyer's patches cells, and combinations thereof.

106. A method of treating a patient for a disease condition, wherein the method comprises:

culturing peripheral lymphoid organ cells on a three-dimensional scaffolding which is covered or surrounded with culture medium under conditions effective to generate and maintain mature and functional peripheral lymphoid organ cells, wherein said three-dimensional scaffolding allows cells in the culture medium to have cell to cell contact in three dimensions; and

administering to a patient an effective amount of peripheral lymphoid organ cells produced in the three dimensional cell culture system, thereby treating the patient for the disease condition.

107. The method according to claim 106, wherein the mammalian peripheral lymphoid organ cells are B-cells, T-cells, or combinations thereof.

108. The method according to claim 107, wherein the mammalian peripheral lymphoid organ cells are T-cells.

109. The method according to claim 106, wherein said culturing is carried out with an antigen or antigenic fragment thereof in the culture medium and under conditions effective to produce antigen-specific lymphocytes.

110. The method according to claim 109, further comprising:
adding an adjuvant to the cell culture.

111. The method according to claim 109, wherein the antigen is selected from the group consisting of a peptide, a protein, a glycoprotein, a proteoglycan, a lipopolysaccharide, a virus, cell, a cell fragment, tissue, and combinations thereof.

112. The method according to claim 111, wherein the antigen is a tumor antigen.

113. The method according to claim 109, wherein said culturing is carried out under conditions effective to permit the antigen-specific lymphocytes to produce antibodies.

114. The method according to claim 109 further comprising:
immortalizing the antigen-specific lymphocytes.

115. The method according to claim 114, wherein said immortalizing is induced.

116. The method according to claim 115, wherein said immortalizing comprises:
fusing the antigen-specific lymphocytes to a cell line under conditions effective to produce a hybridoma cell line.

117. A method of treating a patient for a disease condition wherein the method comprises:
administering to a patient an effective amount of an antibody produced according to claim 31, thereby treating the patient for the disease condition.

118. A method of treating a patient for a disease condition, wherein the method comprises:

administering to a patient an effective amount of an antibody produced according to claim 36, thereby treating the patient for the disease condition.

119. A method for effecting gene expression of peripheral lymphoid organ cells, said method comprising:

culturing peripheral lymphoid organ cells on a three-dimensional scaffolding which is covered or surrounded with culture medium under conditions effective to generate and maintain mature and functional peripheral lymphoid organ cells, wherein said three-dimensional scaffolding allows cells in the culture medium to have cell to cell contact in three dimensions; and

transforming or transducing the cultured peripheral lymphoid organ cells with a desired gene, thereby effecting gene expression of the peripheral lymphoid organ cells.

120. A method of treating a patient for a disease condition, said method comprising:

administering to a patient an effective amount of the transformed or transduced the cultured peripheral lymphoid organ cells according to claim 119, thereby treating the patient for the disease condition.